



ocket No. 1443.008US1
WD #437013

KC Ref. No. 16626

CLEAN VERSION OF PENDING CLAIMS

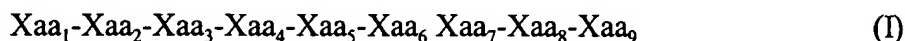
METALLOPROTEINASE INHIBITORS FOR WOUND HEALING

Applicant: Stephen Quirk

Serial No.: 10/032,376

1. A peptide comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, or SEQ ID NO:17, wherein the peptide can inhibit matrix metalloproteinase-2.

2. A composition comprising a therapeutically effective amount of peptide of formula I and a pharmaceutically acceptable carrier:



wherein

Xaa₁, Xaa₄, and Xaa₆ are separately each apolar amino acids;

Xaa₂ is a basic amino acid;

Xaa₃ is a cysteine-like amino acid;

Xaa₅ is a polar or aliphatic amino acid;

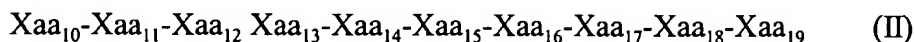
Xaa₇ is an acidic amino acid,

Xaa₈ is an aliphatic or polar amino acid;

Xaa₉ is an aliphatic, apolar or basic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

3. A composition comprising a therapeutically effective amount of peptide of formula II and a pharmaceutically acceptable carrier:



wherein

Xaa₁₀ is a polar, acidic, basic or apolar amino acid;

Xaa₁₁ is a polar or aromatic amino acid;

Xaa₁₂ is a polar, basic, aliphatic or apolar amino acid ;

Xaa₁₃ is an aromatic, aliphatic, polar or acidic amino acid;

Xaa₁₄ is an aromatic, apolar or polar amino acid;

Xaa₁₅ is an apolar or acidic amino acid;

Xaa₁₆ is a basic, a polar or an apolar amino acid;

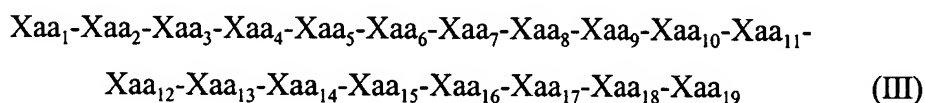
Xaa₁₇ is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;

Xaa₁₈ is an apolar or an aliphatic amino acid;

Xaa₁₉ is a basic or an aliphatic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

4. A composition comprising a therapeutically effective amount of peptide of formula III and a pharmaceutically acceptable carrier:



wherein

Xaa₁, Xaa₄, and Xaa₆ are separately each apolar amino acids;

Xaa₂ is a basic amino acid;

Xaa₃ is a cysteine-like amino acid;

Xaa₅ is a polar or aliphatic amino acid;

Xaa₇ is an acidic amino acid;

Xaa₈ is an aliphatic or polar amino acid;

Xaa₉ is an aliphatic, apolar or basic amino acid;

Xaa₁₀ is a polar, acidic, basic or apolar amino acid;

Xaa₁₁ is a polar or aromatic amino acid;

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Xaa₁₂ is a polar, basic, aliphatic or apolar amino acid;

Xaa₁₃ is an aromatic, aliphatic, polar or acidic amino acid;

Xaa₁₄ is an aromatic, apolar or polar amino acid;

Xaa₁₅ is an apolar or acidic amino acid;

Xaa₁₆ is a basic, a polar or an apolar amino acid;

Xaa₁₇ is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;

Xaa₁₈ is an apolar or an aliphatic amino acid;

Xaa₁₉ is a basic or an aliphatic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

5. (Amended) A composition that comprises a therapeutically effective amount of peptide of formula IV and a pharmaceutically acceptable carrier:

Xaa_a-Xaa_b-Xaa_c-Xaa_d-Xaa_e-Xaa_f-Xaa_g-Xaa_h-Xaa_i-Xaa_j-Xaa_k-Xaa_l-Xaa_m-

Xaa₁-Xaa₂-Xaa₃-Xaa₄-Xaa₅-Xaa₆-Xaa₇-Xaa₈-Xaa₉-Xaa₁₀-Xaa₁₁-

Xaa₁₂-Xaa₁₃-Xaa₁₄-Xaa₁₅-Xaa₁₆-Xaa₁₇-Xaa₁₈-Xaa₁₉ (IV)

(SEQ ID NO:18)

wherein:

Xaa_a is proline;

Xaa_b is glutamine or glutamic acid;

Xaa_c is threonine;

Xaa_d is glycine;

Xaa_e is aspartic acid or glutamic acid;

Xaa_f is leucine;

Xaa_g is aspartic acid;

Xaa_h is glutamine or serine;

Xaa_i is proline;

Xaa_j is arginine;

Xaa_k is cysteine;

Xaa_l is glycine;

Xaa₅ is valine or asparagine;

Xaa₆ is proline;

Xaa₇ is aspartic acid;

Xaa₈ is valine or leucine;

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Xaa _i is asparagine or alanine;	Xaa ₉ is alanine or glycine;
Xaa _j is threonine;	Xaa ₁₀ is asparagine or arginine;
Xaa _k is isoleucine or leucine;	Xaa ₁₁ is tyrosine or phenylalanine;
Xaa _l is glutamic acid or lysine;	Xaa ₁₂ is asparagine or glutamine;
Xaa _m is threonine or alanine;	Xaa ₁₃ is phenylalanine or threonine;
Xaa _n is methionine;	Xaa ₁₄ is phenylalanine;
Xaa _o is arginine;	Xaa ₁₅ is proline or glutamic acid;
Xaa _p is lysine or threonine;	Xaa ₁₆ is arginine or glycine;
Xaa ₁₇ is lysine or aspartic acid;	Xaa ₁₈ is proline or leucine;
Xaa ₁₉ is lysine; and	

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

6. The composition of any one of claims 2-5, wherein an apolar amino acid is methionine, glycine or proline.
7. The composition of any one of claims 2-5, wherein a basic amino acid is histidine, lysine, arginine, 2,3-diaminopropionic acid, ornithine, homoarginine, ρ -aminophenylalanine, and 2,4-diaminobutyric acid.
8. The composition of any one of claims 2-5, wherein a cysteine-like amino acid is cysteine, homocysteine, penicillamine, or β -methyl cysteine.
9. The composition of any one of claims 2-5, wherein an aliphatic amino acid is alanine, valine, leucine, isoleucine, t-butylalanine, N-methylisoleucine, norleucine, N-methylvaline, cyclohexylalanine, β -alanine, N-methylglycine, or α -aminoisobutyric acid.

10. The composition of any one of claims 2-5, wherein an acidic amino acid is aspartic acid or glutamic acid.
11. The composition of any one of claims 2-5, wherein a polar amino acid is asparagine, glutamine, serine, threonine, tyrosine, citrulline, N-acetyl lysine, methionine sulfoxide, or homoserine, or an apolar amino acid such as methionine, glycine or proline.
12. The composition of any one of claims 2-5, wherein an aromatic amino acid is phenylalanine, tyrosine, tryptophan, phenylglycine, naphthylalanine, β -2-thienylalanine, 1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid, 4-chlorophenylalanine, 2-fluorophenylalanine, 3-fluorophenylalanine, 4-fluorophenylalanine, pyridylalanine, or 3-benzothienyl alanine.
13. (Amended) The composition of any one of claims 2-5 wherein the matrix metalloproteinase is any one of matrix metalloproteinase-1, matrix metalloproteinase-2, matrix metalloproteinase-3, matrix metalloproteinase-4, matrix metalloproteinase-5, matrix metalloproteinase-6, matrix metalloproteinase-7, matrix metalloproteinase-8, and matrix metalloproteinase-9, matrix metalloproteinase-10, matrix metalloproteinase-11, matrix metalloproteinase-12, or matrix metalloproteinase-13.
14. A composition that comprises a therapeutically effective amount of peptide that comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13, and a pharmaceutically acceptable carrier.
15. (Amended) The composition of claim 14 wherein the peptide can inhibit proteinase activity of any one of matrix metalloproteinase-1, matrix metalloproteinase-2, matrix

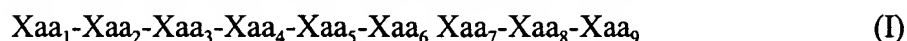
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metalloproteinase-3, matrix metalloproteinase-4, matrix metalloproteinase-5, matrix metalloproteinase-6, matrix metalloproteinase-7, matrix metalloproteinase-8, and matrix metalloproteinase-9, matrix metalloproteinase-10, matrix metalloproteinase-11, matrix metalloproteinase-12, or matrix metalloproteinase-13.

16. A wound dressing that comprises a peptide of the formula I:



wherein

Xaa₁, Xaa₄, and Xaa₆ are separately each apolar amino acids;

Xaa₂ is a basic amino acid;

Xaa₃ is a cysteine-like amino acid;

Xaa₅ is a polar or aliphatic amino acid;

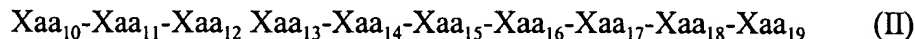
Xaa₇ is an acidic amino acid,

Xaa₈ is an aliphatic or polar amino acid;

Xaa₉ is an aliphatic, apolar or basic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

17. A wound dressing that comprises a peptide of the formula II:



wherein

Xaa₁₀ is a polar, acidic, basic or apolar amino acid;

Xaa₁₁ is a polar or aromatic amino acid;

Xaa₁₂ is a polar, basic, aliphatic or apolar amino acid ;

Xaa₁₃ is an aromatic, aliphatic, polar or acidic amino acid;

Xaa₁₄ is an aromatic, apolar or polar amino acid;

Xaa₁₅ is an apolar or acidic amino acid;

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Xaa₁₆ is a basic, a polar or an apolar amino acid;

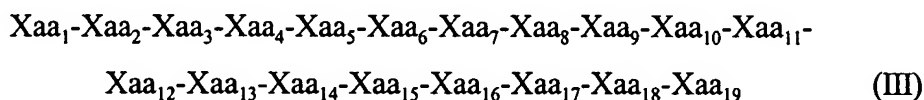
Xaa₁₇ is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;

Xaa₁₈ is an apolar or an aliphatic amino acid;

Xaa₁₉ is a basic or an aliphatic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

18. A wound dressing that comprises a peptide of formula III:



wherein

Xaa₁, Xaa₄, and Xaa₆ are separately each apolar amino acids;

Xaa₂ is a basic amino acid;

Xaa₃ is a cysteine-like amino acid;

Xaa₅ is a polar or aliphatic amino acid;

Xaa₇ is an acidic amino acid;

Xaa₈ is an aliphatic or polar amino acid;

Xaa₉ is an aliphatic, apolar or basic amino acid;

Xaa₁₀ is a polar, acidic, basic or apolar amino acid;

Xaa₁₁ is a polar or aromatic amino acid;

Xaa₁₂ is a polar, basic, aliphatic or apolar amino acid;

Xaa₁₃ is an aromatic, aliphatic, polar or acidic amino acid;

Xaa₁₄ is an aromatic, apolar or polar amino acid;

Xaa₁₅ is an apolar or acidic amino acid;

Xaa₁₆ is a basic, a polar or an apolar amino acid;

Xaa₁₇ is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;

Xaa₁₈ is an apolar or an aliphatic amino acid;

Xaa₁₉ is a basic or an aliphatic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

19. (Amended) A wound dressing that comprises a peptide of formula IV:

Xaa_a-Xaa_b-Xaa_c-Xaa_d-Xaa_e-Xaa_f-Xaa_g-Xaa_h-Xaa_i-Xaa_j-Xaa_k-Xaa_l-Xaa_m-

Xaa₁-Xaa₂-Xaa₃-Xaa₄-Xaa₅-Xaa₆-Xaa₇-Xaa₈-Xaa₉-Xaa₁₀-Xaa₁₁-

Xaa₁₂-Xaa₁₃-Xaa₁₄-Xaa₁₅-Xaa₁₆-Xaa₁₇-Xaa₁₈-Xaa₁₉ (IV)

(SEQ ID NO:18)

wherein:

Xaa_a is proline;

Xaa_b is glutamine or glutamic acid;

Xaa_c is threonine;

Xaa_d is glycine;

Xaa_e is aspartic acid or glutamic acid;

Xaa_f is leucine;

Xaa_g is aspartic acid;

Xaa_h is glutamine or serine;

Xaa_i is asparagine or alanine;

Xaa_j is threonine;

Xaa_k is isoleucine or leucine;

Xaa_l is glutamic acid or lysine;

Xaa_m is threonine or alanine;

Xaa_n is methionine;

Xaa_o is arginine;

Xaa_p is lysine or threonine;

Xaa₁ is proline;

Xaa₂ is arginine;

Xaa₃ is cysteine;

Xaa₄ is glycine;

Xaa₅ is valine or asparagine;

Xaa₆ is proline;

Xaa₇ is aspartic acid;

Xaa₈ is valine or leucine;

Xaa₉ is alanine or glycine;

Xaa₁₀ is asparagine or arginine;

Xaa₁₁ is tyrosine or phenylalanine;

Xaa₁₂ is asparagine or glutamine;

Xaa₁₃ is phenylalanine or threonine;

Xaa₁₄ is phenylalanine;

Xaa₁₅ is proline or glutamic acid;

Xaa₁₆ is arginine or glycine;

Xaa₁₇ is lysine or aspartic acid;

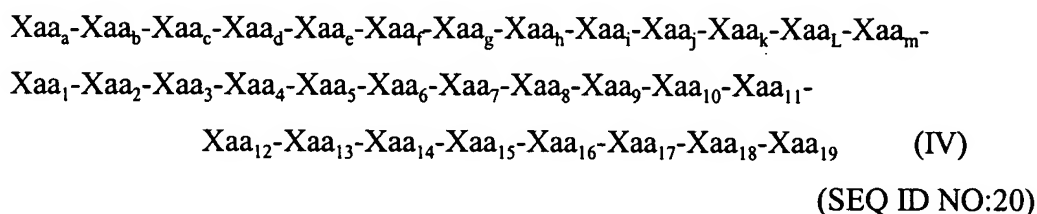
Xaa₁₈ is proline or leucine;

Xaa₁₉ is lysine; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

20. (Amended) The wound dressing of any one of claims 16-19 or 28, wherein an apolar amino acid is methionine, glycine or proline.
21. (Amended) The wound dressing of any one of claims 16-19 or 28, wherein a basic amino acid is histidine, lysine, arginine, 2,3-diaminopropionic acid, ornithine, homoarginine, ρ -aminophenylalanine, and 2,4-diaminobutyric acid.
22. (Amended) The wound dressing of any one of claims 16-19 or 28, wherein a cysteine-like amino acid is cysteine, homocysteine, penicillamine, or β -methyl cysteine.
23. (Amended) The wound dressing of any one of claims 16-19 or 28, wherein an aliphatic amino acid is alanine, valine, leucine, isoleucine, t-butylalanine, N-methylisoleucine, norleucine, N-methylvaline, cyclohexylalanine, β -alanine, N-methylglycine, or α -aminoisobutyric acid.
24. (Amended) The wound dressing of any one of claims 16-19 or 28, wherein an acidic amino acid is aspartic acid or glutamic acid.
25. (Amended) The wound dressing of any one of claims 16-19 or 28, wherein a polar amino acid is asparagine, glutamine, serine, threonine, tyrosine, citrulline, N-acetyl lysine, methionine sulfoxide, or homoserine, or an apolar amino acid such as methionine, glycine or proline.

26. (Amended) The wound dressing of any one of claims 16-19 or 28, wherein an aromatic amino acid is phenylalanine, tyrosine, tryptophan, phenylglycine, naphthylalanine, β -2-thienylalanine, 1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid, 4-chlorophenylalanine, 2-fluorophenylalanine, 3-fluorophenylalanine, 4-fluorophenylalanine, pyridylalanine, or 3-benzothienyl alanine.
27. A wound dressing that comprises a peptide comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13, wherein the peptide can inhibit a matrix metalloproteinase.
28. (New) A composition that comprises a therapeutically effective amount of peptide of formula IV and a pharmaceutically acceptable carrier:



wherein:

- Xaa₁, Xaa₄, and Xaa₆ are separately each apolar amino acids;
- Xaa₂ is a basic amino acid;
- Xaa₃ is a cysteine-like amino acid;
- Xaa₅ is a polar or aliphatic amino acid;
- Xaa₇ is an acidic amino acid,
- Xaa₈ is an aliphatic or polar amino acid;

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Xaa₉ is an aliphatic, apolar or basic amino acid; and
 Xaa₁₀ is a polar, acidic, basic or apolar amino acid;
 Xaa₁₁ is a polar or aromatic amino acid;
 Xaa₁₂ is a polar, basic, aliphatic or apolar amino acid ;
 Xaa₁₃ is an aromatic, aliphatic, polar or acidic amino acid;
 Xaa₁₄ is an aromatic, apolar or polar amino acid;
 Xaa₁₅ is an apolar or acidic amino acid;
 Xaa₁₆ is a basic, a polar or an apolar amino acid;
 Xaa₁₇ is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;
 Xaa₁₈ is an apolar or an aliphatic amino acid;
 Xaa₁₉ is a basic or an aliphatic amino acid;
 Xaa_a is proline;
 Xaa_b is glutamine or glutamic acid;
 Xaa_c is threonine;
 Xaa_d is glycine;
 Xaa_e is aspartic acid or glutamic acid;
 Xaa_f is leucine;
 Xaa_g is aspartic acid;
 Xaa_h is glutamine or serine;
 Xaa_i is asparagine or alanine;
 Xaa_j is threonine;
 Xaa_k is isoleucine or leucine;
 Xaa_l is glutamic acid or lysine;
 Xaa_m is threonine or alanine;
 Xaa_n is methionine;
 Xaa_o is arginine;

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Xaa_p is lysine or threonine; and
wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.